

R E M A R K S

All amendments and cancellation of claims are made without acquiescing to any of the Examiner's arguments or rejections, and solely for the purpose of expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG),¹ and without waiving the right to prosecute the cancelled claims (or similar claims) in the future.

In the Office Action dated 9/12/06, the Examiner issued 3 rejections under 35 U.S.C. 103. Each of the rejections is discussed in detail below.

I. Claims 1-15 are Non Obvious

The Examiner rejects Claims 1-15 under 35 U.S.C. 103 as allegedly being obvious in light of Hanash et al. (US 2003/0013138; hereinafter Hanash) in light of Schneider et al. (U.S. Patent 6,537,432, hereinafter Schneider). The Applicants respectfully disagree with the rejection. However, in order to further the business interests of the Applicants and while reserving the right to prosecute the original (or similar) claims in the future, the Applicants have amended Claim 1 to include the elements of dependent Claims 12-15. The amended Claim 1 includes the elements of comparing the proteomes of cancerous and non-cancerous cells.

The Applicants respectfully disagree with the rejection. *A prima facie* case of obviousness requires the Office to cite a reference, or combination of references, that (a) discloses all of the elements of the claimed invention, (b) provides a suggestion or motivation to one of skill in the art to combine the elements to yield the claimed combination, and (c) provides a reasonable expectation of successfully carrying out the claimed combination. Failure to establish any one of the three requirements precludes a finding of a *prima facie* case of obviousness, and, without more, entitles the Applicants to allowance of the claims at issue.² The Examiner has failed to establish a *prima facie* case of obviousness because 1) the Examiner has not provided a motivation to combine the references; 2) the Examiner is applying hindsight reconstruction; and 3) the Examiner has not demonstrated a reasonable expectation of success,

¹ 65 Fed. Reg. 54603 (Sept., 8, 2000).

² See, e.g., *Northern Telecom Inc. v. Datapoint Corp.*, 15 USPQ2d 1321, 1323 (Fed. Cir. 1990).

should the combination be carried out.

**1. There Is No Motivation To Combine The References In The Manner
Indicated By The Examiner**

The Examiner fails to provide any proper evidence of a motivation to combine the Hanash and Schneider references, thus a *prima facie* case of obviousness has not been established. The Hanash reference cited by the Examiner is specifically directed towards fractionating proteomes, rather than analysis of entire proteomes. Hanash specifically teaches away from separation of entire proteomes:

“For Example, the present invention provides methods of tagging membrane proteins to allow separation and/or characterization of the membrane proteins. In some embodiments, the systems and methods of the present invention allow the characterization of rare proteins that would be undetectable if analyzed along with the entire proteome of a cell.” (Paragraph 0046)

In addition, as the Examiner has admitted, the Hanash reference does not teach or suggest analysis of proteins by size. The Hanash reference further does not teach or suggest the specific order and types of separations utilized in the present invention. The Schneider reference does not teach or suggest the analysis of an entire proteome through multiple separation steps. Indeed, Schneider specifically teaches away from the analysis of entire proteomes: “During the elution or withdrawing of resolved proteins, generally only a portion of the electrophoretic medium containing the resolved proteins is typically collected in any given fraction.” (Column 9, 3rd paragraph). Schneider further does not teach or suggest the specific order and types of separations utilized in the present invention.

The Applicants submit that the Examiner has failed to provide the required motivation to combine the teachings of Hanash and Schneider. The mere fact that the methods of Hanash or Schneider could be used in the analysis of proteomes does not relieve the Examiner of his burden to provide some motivation from within the teachings of Hanash or Schneider to combine the references to arrive at the presently claimed invention. Nor has the Examiner provided a motivation from the knowledge of a person of ordinary skill in the art. The Applicants request that the Examiner point to a motivation, either from within the teachings, or from one of ordinary skill in the art (e.g., a declaration of one of ordinary skill in the art at the time of filing of the

present invention).

The Examiner thus appears to *assume* that such motivation exists in the "general knowledge," without providing any basis for such an assumption. As discussed above, however, the requisite motivation must be found either in the prior art or in knowledge that is generally available to those of ordinary skill in the art; a baseless *assumption* of such knowledge is legally impermissible under *Fine* and *Kotzhab*. Moreover, as the Federal Circuit has held:

[t]he range of sources available, however, does not diminish the requirement for actual evidence. That is, the showing must be clear and particular. Broad conclusory statements regarding the teaching of multiple references, standing alone, are not "evidence."

In re Dembiczak, 175 F.3d 994, 999 (Fed. Cir. 1999) (citations omitted). Since the Examiner has provided no actual evidence to support the conclusory statement that the cited references in combination render the present invention obvious, Applicants respectfully assert that a *prima facie* case of obviousness has not been established.

The Office has also failed to analyze the invention as a whole. When analyzed as a whole, the specific combination and order of separation steps of the presently claimed invention is non-obvious. "That each element in a claimed invention is old or unpatentable does not determine the nonobviousness of the claimed invention as a whole." *Custom Accessories v. Jeffrey-Allan Industries Inc.*, 807 F.2d 955, 1 USPQ 2d 1196, 1198 (Fed. Cir. 1986); See also *Brantingson Fishing Equipment Co. v. Shimano American Corp.*, 9 USPQ 2d 1669, 1672 (Fed. Cir. 1988). Put another way: "Only God works from nothing. Men must work with old elements." *Fromson v. Advance Offset Plate, Inc.*, 755 F.2d 1549, 225 USPQ 26, 31 n. 3 (Fed. Cir. 1985) (quoting from Markey, "Why Not the Statute," 65 JPOS 331, 333-334 (1983)).

The *Fromson* case is particularly relevant here. In that case, the inventor developed a process for photolithography using 1) aluminum as a substrate, 2) oxide coatings by anodization, 3) silication, and 4) application of light-sensitive resins. The district court correctly found that each of these elements individually were known in the art - but incorrectly concluded, on the basis of the unpatentability of each element, that the combination of these steps was unpatentable. On appeal, the Federal Circuit pointed to the "fundamental error" of the district court, noting: "At no point did the court indicate, nor does the record indicate, a basis on which it can be said that the making of that combination would have been obvious when it was made."

Fromson, supra at 31.

Likewise, in the instant case there has been no showing of why one would be motivated to combine the teachings of Hanash and Schneider to arrive at the presently claimed invention. Absent a motivation to combine the references, the Office has not established a prima facie case of obviousness.

2. The Office's Reasoning is Based on Improper Hindsight Reconstruction

The Applicants submit that the Office has improperly applied hindsight reconstruction to combine the Hanash and Schneider references. The Examiner has found the alleged motivation to combine the cited references in Applicants' own specification rather than in the cited art or from knowledge within the art. Specifically, to arrive at the presently claimed invention, one of ordinary skill in the art would have had to have been motivated to: (I) choose the separation methods of Hanash, while ignoring the fact that Hanash says nothing about (and, indeed, is not at all concerned with) separation based on size, and separation of whole proteomes (where Hanash teaches the opposite-fractionating proteomes); and combine these elements with (II) the separation methods of Schneider, while ignoring the fact that Schnieder does not teach or suggest the use of the described methods for analysis of entire proteomes in the order described by the presently claimed invention. Without using the presently claimed invention and the present specification as the blueprint for this hindsight "picking and choosing" of the isolated elements of each reference, one of ordinary skill in the art would have found no specific suggestions to include one element and exclude another from each of the cited references to produce the presently claimed invention. Without such suggestions in the cited art, the combination of the cited references as the Examiner has done is nothing more than a hindsight obviousness analysis.

As the Federal Circuit has held numerous times, however, such a hindsight analysis is impermissible -- instead, the Examiner must show suggestions, explicit or otherwise, that would compel one of ordinary skill to combine the cited references in order to make and use the claimed invention. *See, e.g., Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 1143 (Fed. Cir. 1985) ("When prior art references require selective combination by the [fact-finder] to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight

gleaned from the invention itself."); *Fine*, 5 USPQ2d at 1600 ("One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention."); *In re Pleuddemann*, 910 F.2d 823, 828 (Fed. Cir. 1990) (noting that use of an applicant's specification as though it were prior art to support an obviousness determination is legal error); *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991) (holding that both the suggestion to combine references, and a reasonable expectation of success in making the claimed invention, "must be founded in the prior art, not in the applicant's disclosure."). The Board has also provided the same mandate on this issue:

it is impermissible to use the claimed invention as an instruction manual or "template" to piece together isolated disclosures and teachings of the prior art so that the claimed invention may be rendered obvious a rejection based on § 103 must rest on a factual basis, with the facts being interpreted without hindsight reconstruction of the invention from the prior art. In making this evaluation, the examiner has the initial duty of supplying the factual basis for the rejection he advances. He may not, because he doubts that the invention is patentable, resort to speculation, unfounded assumptions or hindsight reconstruction to supply deficiencies in the factual basis.

Ex parte Haymond, 41 USPQ2d 1217, 1220 (Bd. Pat. App. Int. 1996). Thus, the use of hindsight analysis in the present case is impermissible and cannot be used to attempt to establish a *prima facie* case of obviousness. Applicants also are well-aware of the often-cited language in the MPEP that:

[a]ny judgement [sic] on obviousness is in a sense necessarily a reconstruction based on hindsight reasoning, but so long as it takes into account only knowledge which was within the level of ordinary skill in the art at the time the claimed invention was made and does not include knowledge gleaned only from applicant's disclosure, such a reconstruction is proper.

MPEP § 2145(X)(A) (quoting *In re McLaughlin*, 443 F.2d 1392, 1395, 170 USPQ 209, 212 (C.C.P.A. 1971)). This boilerplate from the MPEP, however, does not negate the Examiner's burden of providing *specific* evidence or knowledge that would have motivated one of ordinary skill to have modified the cited references and combine their respective disclosures so as to arrive at the presently claimed invention. As noted above, such specific evidence or knowledge has not been provided by the Examiner; hence, the boilerplate language from the MPEP is of no avail in

the present case.

Moreover, it is axiomatic that, in order to support a *prima facie* case of obviousness, the prior art must suggest making the *specific* modifications necessary to achieve the claimed invention. See *In re Deuel*, 51 F.3d 1552, 1558 (Fed. Cir. 1995); *In re Lahu*, 747 F.2d 703, 705 (Fed. Cir. 1984) ("[t]he prior art must provide one of ordinary skill in the art the motivation to make the proposed molecular modifications needed to arrive at the claimed compound."). That is, simply because "one can conceive a general process in advance for generating an *undefined* method [e.g., separating and analyzing proteomes] does not mean that a claimed *specific* method [e.g., the specific methods of the presently claimed invention] was precisely envisioned and therefore obvious." *Deuel* at 1559. Thus, in order for Hanash and Schneider to be suitable as primary references upon which to base a *prima facie* case of obviousness, there must be, at a minimum, a teaching or suggestion in these references or in the art that would have compelled one of ordinary skill in the art to include all of the elements of the presently claimed invention in the combination of the presently claimed invention. As noted above, such a teaching or suggestion is wholly lacking in Hanash and Schneider. Therefore, the cited references taken together are seriously deficient (particularly in view of the holding in *Deuel*), and cannot support a *prima facie* case of obviousness.

3. The Cited references do not provide a reasonable expectation of Success

Even if the cited references are improperly combined, the cited references do not provide an expectation of success, should the combination be carried out. As stated in the present specification, the specific combination and order of separation steps described by the claimed invention is preferred in order to obtain high resolution proteomic separations:

"Initial experiments conducted during the course of development of the present invention resulted in the conclusion that use of protein size based separations in the first dimension achieved poor resolution of complex mixtures such that a unique form of a protein was localized to a relatively large number of fractions, creating difficulty in achieving adequate resolution in the three-dimensional separation system. Further experiments indicated that the use of reverse phase chromatography for the first dimension separation was difficult to achieve with conventional columns because of the need to separate large amounts of protein in complex mixtures. Additionally, poor recovery of proteins off the column was observed." (Specification, pg. 15, lines 2-10).

Neither Hanash, nor Schneider, alone or in combination, teach or suggest that the order of separation steps is necessary for successful separations. Nor do Hanash or Schneider teach or suggest the specific separations or order of separations described by the presently claimed invention. As such, the Applicants submit that the Examiner has not demonstrated a reasonable expectation of success. Accordingly, the Applicants request that the rejection be withdrawn.

II. Claims 1-7 and 12-13 are Non-Obvious

The Examiner rejects Claims 1-7 and 12-13 under 35 U.S.C. 103 as allegedly being obvious in light of Lubman et al (US 2002/0098595; hereinafter Lubman) in light of Schneider. The Applicants respectfully disagree with the rejection. The Examiner has failed to establish a *prima facie* case of obviousness because 1) the Examiner has not provided a motivation to combine the references; 2) the Examiner is applying hindsight reconstruction; and 3) the Examiner has not demonstrated a reasonable expectation of success, should the combination be carried out.

In particular, the Applicants submit that Lubman does not provide a motivation to combine the described separation methods with those of Schneider. As the Examiner has admitted, the Lubman reference does not teach or suggest analysis of proteins by size or a need for such separations. The Lubman reference further does not teach or suggest the specific order and types of separations utilized in the present invention. The Schneider reference does not teach or suggest the analysis of an entire proteome through multiple separation steps. Indeed, as described above, Schneider specifically teaches away from the analysis of entire proteomes. As such, the Applicants submit that the Examiner has not demonstrated a *prima facie* case of obviousness. As described above, the Examiner is instead relying on a hindsight analysis. The Applicants have not reiterated the relevant case law but instead refer the Examiner to the above discussion of improper hindsight analysis.

Even if the cited references are improperly combined, the cited references do not provide an expectation of success, should the combination be carried out. As described above, the present specification states that the specific combination and order of separation steps described by the claimed invention is preferred in order to obtain high resolution proteomic separations. Neither Lubman, nor Schneider, alone or in combination, teach or suggest that the order of

separation steps in necessary for successful separations. Nor do Lubman or Schneider teach or suggest the specific separations or order of separations of the presently claimed invention. As such, the Applicants submit that the Examiner has not demonstrated a reasonable expectation of success. Accordingly, the Applicants request that the rejection be withdrawn.

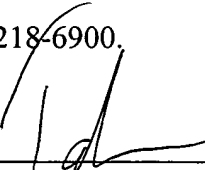
III. Claims 8-11 are Non-Obvious

The Examiner rejects Claims 8-11 under 35 U.S.C. 103 as allegedly being obvious in light of Lubman in light of Schneider and further in view of Hanash. The Applicants respectfully disagree with the rejection. The Examiner has failed to establish a *prima facie* case of obviousness. As described above, Claim 1 is non-obvious in light of Lubman in view of Schneider and Hanash in view of Schneider. Claims 8-11 depend on Claim 1. Thus, if Claim 1 is non-Obvious, Claims 8-11 are non-obvious. The combination of Lubman, Schneider and Hanash does not provide a motivation to combine the cited references with a reasonable expectation of success to arrive at Claim 1 (see above arguments). As such, Claim 1 is non-obvious and Claims 8-11 are also non-obvious. As such, the Applicants respectfully request that the rejection be withdrawn.

CONCLUSION

If a telephone interview would aid in the prosecution of this application, the Examiner is encouraged to call the undersigned collect at (618) 218-6900.

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